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Association Between Primary Open-Angle Glaucoma and Serum Lipid Profile

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Abstract
Globally, glaucoma is the most common cause of irreversible blindness. Primitive Open Angle Glaucoma (POAG) typically exhibits no symptoms until the illness reaches an advanced stage. One of the main risk factors for the development of POAG is intraocular pressure (IOP). However, some instances continue to proceed despite IOP management, supporting the hypothesis that the pathophysiology of glaucoma must involve additional independent risk factors. Contradictory results from recent epidemiological research have raised the possibility that hyperlipidemia and glaucoma are related. To determine the association between serum lipid levels and primary open-angle glaucoma. The current study was a case-control study with a total of 80 subjects, including 40 patients with POAG documented by an array of clinical tests and 40 age-matched controls, conducted in the department of Ophthalmology, Sree Mookambika Institute of Medical Sciences. All patients underwent ophthalmic examinations. Total cholesterol, triglycerides (TG), low density lipoproteins (LDL) and high density lipoproteins (HDL) were measured as part of a fasting lipid profile. Using SPSS 24 software, statistical analysis was carried out using the chi square and unpaired t-tests. A p-value of less than 0.05 was considered significant. The mean age of the patients was 63.45±4.56 while that of the controls was 61.78±5.17 ($p = 0.103$). High total cholesterol levels (>200 mg/dl) were found in 20 (50%) cases and 8 (20%) controls. High serum triglyceride levels (>150 mg/dl) were found in 19 (47.5%) cases and 13 (32.5%) controls. High LDL levels (130 mg/dl) were found in 24 (60%) cases and 12 (30%) controls. Low HDL levels (<40 mg/dl) were found in 15 (37.5%) cases and 3 (7.5%) controls. As for the mean serum triglyceride levels, they were 158.66±38.34mg/dl and 139.38±21.57mg/dl, respectively, for the mean LDL levels, they were 139.98±27.88 mg/dl and 116.75±18.56 mg/dl and for the mean HDL levels, they were 36.71±10.05 mg/dl and 42.67±7.77mg/dl, respectively. The mean cholesterol, triglyceride and LDL levels were significantly higher in cases than in controls ($p<0.05$). A substantial correlation has been shown between dyslipidemia and a higher incidence of POAG. Hence, managing dyslipidemia may be a viable prophylactic measure for POAG.

INTRODUCTION

Glaucoma is the second most common cause of blindness in the world. POAG affects more individuals than angle closure glaucoma (ACG) in the world, with a roughly 3:1 ratio and significant population variances[1]. Globally, there will be about 111.8 million cases of glaucoma by 2040. In addition, it is estimated that there are already over 3 million blind individuals, if better screening and efficient treatment approaches are not successful, this number is expected to increase to 3.2 million by 2020 due to rising prevalence[2]. In India, Primary Open-angle glaucoma (POAG) is more prevalent than PACG[3].

POAG is a complex disorder that starts as a neurodegenerative disease and progresses to glaucomatous optic neuropathy, glaucomatous vision field loss and ultimately progressive blindness[4]. About 11 million people in India who are 40 years of age or older suffer from glaucoma. An estimated 6.48 million people are impacted by POAG. High intraocular pressure, alterations in the optic disc and neuro retinal rim, abnormalities in the visual field and an open anterior chamber angle on gonioscopy are all signs of POAG[4,2].

POAG is recognized to be associated to both type 2 diabetes and hypertension. High lipid levels generate atherosclerotic alterations that contribute to hypertension, while diabetes and hypertension are associated with high lipid levels (dyslipidemia and insulin resistance are related). Therefore, there's a chance that serum lipid levels and glaucoma are tangentially related. Raised intraocular pressure, an elevated cup-disc ratio, pseudoexfoliation, myopia, optic disc hemorrhage, peripapillary atrophy and other conditions are examples of ocular risk factors[5].

Disorders in the metabolism of lipid production and breakdown lead to hyperlipoproteinemia. Triglycerides, cholesterol and phospholipids are examples of total lipids. High-density lipoproteins (HDL), low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) are the lipoproteins that carry lipids in the blood. It has been revealed that glaucoma patients with atherosclerosis and elevated intraocular pressure have lower pulse volumes[6].

Increased intraocular pressure (IOP) is the primary risk factor in the context of glaucoma. IOP causes optic nerve damage by two mechanisms: mechanical damage directly to the layer of retinal nerve fibers, or ischemic damage from compression of the blood vessels nourishing the optic nerve head. Ocular perfusion may be impacted by atherosclerotic alterations brought on by excessive cholesterol levels, or trabecular meshwork and endothelium of blood arteries supplying the optic nerve head may be directly damaged by lipid peroxidation leading to oxidative stress[7].

Serum lipid levels and glaucoma have long been thought to be related and numerous studies have found varying degrees of correlation between the two. The earlier findings further suggested that changes in hyperlipidemia levels may have a role in the pathophysiology of different types of glaucoma. Nonetheless, the literature contains contradicting results. According to certain research, there was a lower risk of open-angle glaucoma in people with hyperlipidemia.

These differing results could be caused by different kinds of glaucoma. As a result, this study was conducted to bring more light on the correlation, which would aid in better understanding the pathophysiology of primary open angle glaucoma, its relationship with serum cholesterol and triglyceride levels, as well as its therapy and management.

Aims and Objectives: The study aimed to determine the association between serum lipid levels and primary open-angle glaucoma.

MATERIALS AND METHODS

The present study was a case-control study carried out over the course of a year, from February 2023 to January 2024, at the Sree Mookambika Institute of Medical Sciences in Kulasekharam. There were 80 people in all, 40 of whom were age-matched controls and 40 of whom were patients with POAG as confirmed by various clinical testing. Excluded from the study were patients under the age of 18, those with a history of trauma or ocular surgery prior to the development of glaucoma in the eye, those with high myopia, those with a known diagnosis of diabetes mellitus, those with hypertension, those with thyroid disease and those who were unwilling to participate. Study subjects were classified into two groups.

Group A: Cases of POAG.

Group B: This group included individuals having no glaucoma but attends eye department for defective vision.

All subjects provided written informed consent. Age, gender and occupation were among the demographic details recorded. An examination of the eyes was done. The angle structures were assessed using gonioscopy. Visual field analysis and fundus examination were performed. Raised IOP, alterations in the optic nerve head identified by direct ophthalmoscopy and visual field abnormalities were used to identify POAG.

The International Society of Geographic and Epidemiological Ophthalmology (ISGEO)[8] established the following criteria for the diagnosis of POAG:

untreated IOP of 21 mmHg or higher with a rebound tonometry, open anterior chamber angles on gonioscopy, glaucomatous optic disc changes (increased cup/disc ratio, thinning of the neuroretinal rim, notching) on ophthalmoscopy and 90D lens and glaucoma-specific visual field defects by standard automated perimetry using the Humphrey Visual Field Analyzer.

Based on AAO criteria[9], glaucoma was classified as mild (optic disc cupping without visual field loss), moderate (glaucomatous optic neuropathy and visual field loss not within 50 of fixation), or severe (visual field loss in both hemispheres or within 50 of fixation). Blood samples were drawn after a 12-hour fast in order to measure serum lipids, which were then evaluated using an enzymatic approach (autoanalyzer). The lipid profile consisted of TGL, LDL, HDL and total cholesterol.

The National Cholesterol Education Program: Adult Treatment Panel III (NCEP: ATP III) guidelines[10] provided the reference values for lipids. Hypercholesterolemia is defined as total cholesterol greater than 200 mg/dl, hypertriglyceridemia as TGL greater than 150 mg/dl, LDL greater than 130 mg/dl and HDL less than 40 mg/dl.

Data had been entered into Microsoft Excel 2016 and SPSS 20.0 was used for analysis. While the sex distribution in the two research groups is provided as frequency and percentage, the demographic data are expressed as mean and standard deviation. Subject characteristics were compared between the groups using the independent Student t-test and chi-square test. To compare the lipid levels between the groups, one-way analysis of variance (ANOVA) was employed. A p value less than 0.05 was considered significant.

RESULTS AND DISCUSSIONS

In total, 80 people were enrolled in our study: 40 in the glaucoma group and 40 in the control group. (Table 1) displays the demographic characteristics of the research population. The age range of 50-70 years old was the maximum number of cases and controls. The mean age and sex of the PACG and control patients did not differ statistically ($p>0.05$).

Triglyceride, LDL and cholesterol levels were shown to be higher in cases with significant p values less than 0.05. Though it was not statistically significant, the HDL level was lower in the cases than in the controls ($p = 0.153$). (Table 2).

When comparing the mean levels of cholesterol, triglycerides and LDL to the controls, there was a significant p-value (<0.001) difference in favor of the cases. (Table 3).

Out of the 40 patients in Group A, 10 patients (about 25%) had mild glaucoma, 13 patients (32.5%) had moderate glaucoma and the remaining 17 patients (42.5%) had severe glaucoma. There was a steady rise in the number of cases with increasing glaucoma grades across all blood lipid measures, with the exception of HDL. With a p-value less than 0.05, the distribution of the various grades of POAG varied significantly depending on the levels of LDL, triglycerides and total cholesterol.

Dyslipidemia has been linked to a number of eye conditions, including age-related macular degeneration, diabetic and hypertensive retinopathy, and retinal vein occlusion[11]. The authors of the current study sought to ascertain whether serum lipid levels and POAG were related. Therefore, it is plausible that there exists an indirect correlation between serum lipid levels and glaucoma.

There have been reports of potential mechanisms for the development of POAG in patients with hyperlipidemia. These include lipid peroxidation, which can cause oxidative stress and damage to the endothelium and trabecular meshwork of blood vessels that supply the optic nerve head, as well as atherosclerotic changes resulting from dyslipidemia that affects the perfusion of the optic nerve. Overconsumption of fat can raise blood viscosity and episcleral venous pressure, which can reduce aqueous humor outflow. An other explanation for this link could be a hereditary predisposition. Lipid metabolism has been linked to genes like caveolin 1 and ABCA 1, whose loci were found to be significantly correlated with the risk of POAG[12].

The current study found that high serum lipid levels are related with an increased risk of POAG, as well as a positive correlation between POAG and dyslipidemia.

These results are similar to the study conducted by Joshi RS[13] where the authors examined 50 patients with POAG and 50 healthy people and found that the proportion of patients with elevated cholesterol levels and hypertriglyceridemia, as well as the mean levels of cholesterol, LDL and triglyceride, were considerably higher in cases than in controls. Additionally, they observed a favorable correlation between dyslipidemia and POAG.

In a study by Dube[14] 40 patients with POAG and 40 people without glaucoma served as the controls. The study revealed that there was a significant difference ($p<0.05$) in the levels of total cholesterol, total triglycerides and LDL between the cases and the controls. Although it was not statistically significant, the HDL level was lower in the cases than in the controls.

POAG was positively correlated with total cholesterol, total triglycerides and LDL in a case control study by Gupta R[15] and Dave P[16].

Table 1: Demographic parameters among both group

Demographic parameters	Group A	Group B	p-value
Mean Age (Years)	63.45±4.56	61.78±5.17	0.103
Age range (Years)	45-72	43-68	0.069
Gender (Male: Female)	28/12	25/15	0.127

Table 2: Descriptive analysis of serum lipid values among both group

Serum lipid parameters	Group A(%)	Group B(%)	p-value
High total cholesterol (>200mg/dl)	20 (50)	8 (20)	0.033
High LDL(>130mg/dl)	24 (60)	12 (30)	0.041
Low HDL(<40mg/dl)	15 (37.5)	3 (7.5)	0.006
High triglyceride (>150mg/dl)	19 (47.5)	13 (32.5)	0.153

Table 3: Comparison of mean serum lipid values among both group

Serum lipid parameters	Group A	Group B	p-value
Mean total cholesterol (mg/dl)	223.14±25.45	172.05±22.14	0.001
Mean LDL(mg/dl)	139.98±27.88	116.75±18.56	0.018
Mean HDL(mg/dl)	36.71±10.05	42.67±7.77	0.041
Mean triglyceride (mg/dl)	158.66±38.34	139.38±21.57	0.001

Table 4: Distribution of Lipid profile in different grades among POAG patient

Serum lipid parameters	Mild	Moderate	Severe	p-value
High total cholesterol (>200mg/dl)	3(15%)	7(35%)	10(50%)	0.003
High LDL(>130mg/dl)	2(8.33%)	8(3.33%)	14(58.34%)	0.017
Low HDL(<40mg/dl)	4(2.67%)	6(40%)	5(3.33%)	0.061
High triglyceride (>150mg/dl)	2(10.52%)	5(26.32%)	12(63.16%)	0.001

Shao M[17] noted that the PACG group had considerably ($p<0.05$) higher serum levels of LDL-C, TRIG, HDL-C, serum Apolipoprotein A (APOA), serum Apolipoprotein B (APOB), serum Apolipoprotein E (APOE) and lipoprotein(a) (LPa) than the control group. Shaikh R[18] revealed that primary open angle glaucoma was present in 56% of the study's cases with elevated serum cholesterol levels, 52% with elevated triglyceride levels and 60% with elevated LDL levels. Additionally, with a statistically significant p value<0.05, the study observed that the levels of total cholesterol, total triglycerides and LDL were considerably higher in cases than in controls.

High levels of LDL, triglycerides and total cholesterol were found to be significantly associated with various grades of glaucoma in the present study, with p-values less than 0.05. El Habbak AH[19] found a statistically significant weak positive correlation between the TC level and the severity of cases, which is comparable to the current study. Multivariate study revealed that only VLDL was a predictor of POAG, but univariate analysis revealed that TC, TG, LDL and risk ratio I were the predictors of POAG.

The study by Nagaraj SS[20] found that there were no significant variations in the distribution among various grades of POAG in relation to various levels of total cholesterol and LDL, with p-values of 0.202 and 0.123, respectively. With p values of 0.004, 0.05 and 0.017 for low HDL, high triglycerides and high VLDL, respectively, it was statistically significant.

Wu YC[21] in their study found that the three groups had significant variations ($p = 0.02$) in mean serum HDL levels, with the severe group having the lowest mean levels (41±11mg/dl), followed by the moderate group (45±16 mg/dl) and the mild group (50±15mg/dl). Among all Normal-tension glaucoma (NTG) patients, the multivariate regression analysis showed a statistically significant positive correlation ($r = 0.34$, $p = 0.03$) between HDL and retinal nerve fiber layer (RNFL) and a statistically significant negative correlation ($B = -0.16$, $p = 0.03$) between HDL and vertical cup-to-disc ratio (VCDR).

CONCLUSIONS

POAG patients had considerably higher levels of high LDL, high triglycerides and high total cholesterol. Significant differences were seen in the distribution of various POAG grades in relation to different levels of HDL, TG and LDL, with a p-value of less than 0.05. A substantial correlation has been shown between dyslipidemia and a higher incidence of primary open angle glaucoma. The symptoms of POAG can take a long time to appear and patients may suffer significant harm before seeking medical attention. Patients with POAG should have their serum lipid levels examined because this can improve their therapy. This study informs clinicians on using a multifactorial approach to address hyperlipidemia in order to prevent the occurrence of POAG and manage it effectively.

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